

Although the Examiner indicated that it would be obvious to combine the references to achieve the invention of the claims, it is respectfully submitted that such a configuration can not be obvious as explained more fully below.

The cited references provide no teaching or suggestion that they could be combined to achieve a combination ion source, multipole ion guide, and Time-Of-Flight (TOF) mass analyzer. Nothing in the references teaches or suggests such a combination. Yet such a teaching or suggestion is necessary for a rejection under §103. *See e.g., Northern Telcom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 15 U.S.P.Q. 1321 (Fed. Cir. 1990) (“It is insufficient that the prior art disclosed the components of the patented device, either separately or used in other combinations; there must be a teaching, suggestion or incentive to make the combination made by the inventor.”). That suggestion or motivation must be in the reference or the prior art itself. *See e.g., In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990); *In re Dow Chemical*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988). Yet, no such suggestion has been cited within the references or within the prior art to combine an ion source, a multipole ion guide and a Time-Of-Flight mass spectrometer to produce a novel analytical instrument.

Ion sources, even atmospheric pressure ion sources, have been interfaced to Time-Of-Flight mass spectrometers as far back as the 1960s. As a later example, U.S. Patent No. 5,070,240 to Lee (filed August 29, 1990) describes an atmospheric pressure ion source with orthogonal pulsing. But even though such ion source - TOF combinations have been around for years, there is no teaching or suggestion in any of the references relied on of having a multipole ion guide interfaced with a ion source - TOF system.

Moreover, there is also no teaching or suggestion in the cited references as to how they could be combined, as to exactly how such a working configuration could be achieved in practice. The present invention, as recited in all of the pending claims, is directed to an analytical instrument which includes a combination ion source, multipole ion guide, and Time-Of-Flight mass analyzer. The present Applicant engaged in significant research and development to determine how this combination could be accomplished until it succeeded in achieving a successful configuration. As discussed in the grandparent application (which issued as U.S. Patent No. 5,652,427) with respect to Claim 35, the entrance ion optics and

vacuum requirements for each mass analyzer type is quite different and specific ion lens systems must be designed to satisfy the unique entrance requirements of each mass analyzer type. Ion energy, ion energy spread, and primary beam ion trajectory will affect Time-Of-Flight mass resolution and mass measurement accuracy in a manner quite different from other mass analyzer types such as quadrupoles, ion traps, magnetic sectors, and FTMS. The initial energy spread and angular divergence of an ion beam entering the pulsing region of a Time-Of-Flight mass analyzer is more tightly constrained than the ion beam entrance specifications for any other mass analyzer type. As a result, the separate elements in the references can not merely be substituted and combined to achieve the claimed invention. In practice, it is the case that mere substitution and combination to achieve the claimed invention was not possible without further research into how configuration can be accomplished. The cited references provides no evidence at all of such research, nor of any indication that such a combination was ever achieved or could expect to succeed. There is no teaching or suggestion in the art as how to achieve the combination as claimed herein.

For example, Douglas, the primary reference, has no teaching or suggestion at all that his multipole ion guide devices can be combined with a TOF mass analyzer. In fact, before Applicant's invention it appeared to not be a particularly workable or desirable combination. The ion beam exiting a multipole ion guide is not a perfectly parallel ion beam directed along the axis. A perfectly parallel beam is not achievable because ions exiting a multipole ion guide, particularly through higher background pressure collisions, do not originate at a point source. Consequently, chromatic aberrations occur when attempting to focus an ion beam exiting a multipole ion guide with a set of electrostatic lenses. Non parallel ion beams entering quadrupoles or ion traps are acceptable and in the case of ion traps are preferred. But non parallel ion beams entering a TOF pulsing region or TOF tube degrade TOF performance and are not acceptable. It was not obvious to one skilled in the art that a multipole ion guide combined with a TOF would improve performance of an API TOF mass analyzer; what would have been obvious, in fact, was that even if such a workable combination could somehow be achieved in practice that it should likely have degraded performance. In the present invention, in contrast, improved performance was achieved. Douglas 726 and 278

does not mention or teach that such a combination was even possible. The other references relied on also do not teach or suggest, either considered individually or together, the possibility or workability of such a combination.

Accordingly, in view of the above, it is respectfully submitted that the claimed inventions are in fully patentable and allowable form. A favorable response allowing all of the claims is respectfully requested and believed fully warranted.

Dated: February 8, 1999

Respectfully submitted,

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